

→ A "PURE" ORGANIC CHEMIST'S DOWNWARD PATH: CHAPTER 3—"RETIREMENT"

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CHARIMON: . . . Is't you, sir, that knows things?

SOOTHSAYER: *In Nature's infinite book of secrecy
A little I can read.*

SHAKESPEARE, *Antony and Cleopatra*,
Act 1, Scene 2

In the first two chapters [1, 2] I stressed the important roles luck and chance have played in shaping my career. Both will be seen as determinant factors in this final installment as well.

Chapter 2 ended with the transfer of personnel and equipment in 1955 to Selman Waksman's Institute of Microbiology at Rutgers University in New Brunswick, New Jersey, a year before mandatory retirement at Columbia. I had worked with Selman in 1938 on a committee [2, p. 15], and his son Byron and I had become friends during Byron's stay in the laboratory at P. and S. in 1950, when he introduced us to probits and struggled gamely with the second component of complement [3]. At the institute one large laboratory and a smaller adjoining one with an office had been assigned to us, but neither had a chemical hood. I was much touched when Selman offered to give up his own laboratory, the only one with a hood, but his sacrifice was avoided by extension of the ducts and construction of a hood in our larger room. My original intention was to start an immunochemical group under Otto J. Plescia's direction and to pull out after 2 or 3 years. The first part of the plan succeeded, but the congenial atmosphere of the institute, the favorable working conditions, the balance between teaching and research, and, above all, the unselfish and complete willingness of Otto to have his former chief stay on re-

For the opening quotation, the one in chapter 2, and for many hours of patient, helpful listening and suggestions the author is indebted to Elizabeth S. Payne of Worthington, Massachusetts, and to her late husband, John C. Payne, formerly Dean of Education at New York University.

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sulted in my remaining, for 9 years. I had also delayed accepting the proffered, salaried Visiting Professorship of Immunochemistry because I did not wish to abandon a home in New York for a supposedly temporary assignment with rather arduous commuting. A departing Norwegian visitor, however, vacated a small apartment in the owner's house on Freed's egg farm not far from the institute. This made it possible to commute in one direction only on most days. In spite of occasional bad odors when an easterly wind blew, this was a satisfactory arrangement. The Freeds were very friendly and often shared a home-baked cake or a nonlaying chicken with their tenant. There was one untoward occurrence: Mr. and Mrs. Freed went on vacation the day Arne Tiselius, an old friend, came to lecture at the institute. I had asked them to fix up a normally unused bedroom across the hall from my apartment so he could stay overnight. After Arne's lecture and the ensuing dinner, I drove Arne to the egg farm only to find a woman sleeping in the bed. The Freeds hadn't told their caretaker of the intended occupant, so we withdrew silently without even awakening the sleeper and found a room at the hotel for Arne.

As the first winter approached, I could not get a heater for my obsolete 4-cylinder 1939 Oldsmobile and often had to stop and scrape sleet or snow from the windshield before going on. After Charlotte Rosen and I were married and we had rented Professor Whitmer's house in Highland Park when he went to the National Science Foundation, Charlotte often came to New Brunswick with me on Saturday or Sunday. We then had one of the last small Plymouths, reliably acquired secondhand through Mary Loveless, who had worked briefly in the laboratory at P. and S. and had, in her medical practice, cured a Plymouth dealer of an allergy. When parked near the station on College Avenue the car was often covered with snow thrown up by the plows, but there were always members of the avenue's fraternity houses willing to dig us out.

The Institute of Microbiology of Rutgers, the State University of New Jersey, was dedicated, with a separate faculty, in 1954 by Selman A. Waksman, professor of microbiology at the College of Agriculture of the University. After his discovery and patenting of streptomycin and other antibiotics, Selman put most of his royalties into a Foundation for Microbiology and the Rutgers Research and Educational Foundation, the latter mainly for the construction and maintenance of the institute. Selman was, of course, appointed dean of the new Faculty of Microbiology. He chose his faculty and a very able executive secretary, Edward R. Isaacs, and was a wise and considerate administrator. The heads of laboratories, who were free to work on any subject of their choice, were Werner Braun, medical bacteriology and microbial genetics; Vernon Bryson, microbial genetics; Ruth E. Gordon, taxonomy; Vincent

Groupé, virology; Hubert and M. P. (Midge) Lechevalier, actinomycetes and the like; Walter J. Nickerson, microbial biochemistry; Otto J. Plescia, immunochemistry and immunology; Carl P. Schaffner, chemistry of antibiotics; and Adolph Zimmerli, in charge of the pilot plant. There was also an excellent library first presided over by Emma C. Gergely, then by Robert A. Day, who went on after some years to become director of publications for the American Society for Microbiology. During my stay Ekkehard Bautz and his wife brought in molecular biology and Henry and Ruth Vogel enzymology; and Lloyd McDaniel replaced Zimmerli, who retired to his native Switzerland. My friend from Columbia days, Oskar P. Wintersteiner, was an honorary professor and gave occasional lectures after he joined the Squibb Institute for Research.

For our teaching, Otto and I planned a ½-year graduate course in immunochemistry every 2 years: two lectures a week, each followed by an afternoon of laboratory work for about a dozen students, as we could cram in no more. We were much pleased when several of our and other faculties and a few postdocs came to listen to some of the lectures. We usually had small groups of students immunize rabbits with albumin which they had isolated from new-laid eggs and crystallized twice. The antisera were analyzed quantitatively with the recrystallized egg albumin and with “egg globulin” so the students could realize the difficulty of purifying a protein—sometimes there was as much anti-“globulin” as anti-albumin.

Before really settling down at the institute I went to the Orient [2, p. 17] to give lectures and attend the first Asian meeting of the World Federation of United Nations Associations (WFUNA) in Bangkok, with the added task of attempting to persuade several Japanese pharmaceutical companies to pay the royalties with which Selman wished to establish a fund for the exchange of Japanese and American microbiologists. The only meeting with the companies’ representatives, delayed by them until the eve of my departure from Tokyo’s International House whose director was also lawyer for the Waksman interests, was brief and unpleasant. They claimed inability to afford royalties, although selling millions of yens’ worth of streptomycin to China and elsewhere. “Do you own an auto?” I asked each one to find out if their salaries were large. All answered yes. “Most of my friends here on academic salaries can’t afford one,” I said, “and we shall try hard to put you in prison if you don’t pay up.” A settlement was eventually made for about one-half the scheduled amount.

At the WFUNA meeting, my resolution for a peace conference, which Mrs. Roosevelt had helped make acceptable to our UN association, failed to pass. On the day it came up, she and the rest of our delegation went off to Angkor Wat, leaving me alone for an unsuccessful fight with the proponents of unlimited sovereignty. Unexpectedly successful, however.

were six lectures at the medical school of the University of Tokyo under the auspices of Tomio Ogata,¹ professor of serology. A team from the U.S. Army Laboratories, commanded by my friend Louis H. Muschel, attended them with cameras and recording equipment, virtually presenting me with most of the material for a book published shortly afterward [4].

On the way to the Orient I stopped several days in Denver to visit and talk at the medical school of the University of Colorado and to get additional material for the biographical memoir on Florence Sabin which Philip McMaster and I were writing for the National Academy of Sciences. At the dinner after my lecture, I mentioned that I was looking for a postdoctoral co-worker familiar with the chemistry of sugars. The director of one of the medical school's institutes, Roger S. Mitchell, said, "I know just the man for you. Paul Rebers, a recent Ph.D. of Fred Smith's, dislikes his industrial job. His record is in my office; could we go there?" I read his fine record and almost at midnight we called Paul and he agreed to come. Luck was certainly with me that night, for Paul and I worked together for 6 years before he moved on to his present post at the Animal Disease Laboratory of the U.S. Department of Agriculture. Paul was the second of my able one-handed associates. He had lost a hand in an explosion of homemade gunpowder and invented a metal substitute which he worked with the muscles of his arm.

After arriving with his wife, Louise, and a new baby, Paul started work on the structure and immunological properties of the capsular polysaccharide of Pn (pneumococcal) type VI. We had a stock of type-specific Pn polysaccharides prepared at E. R. Squibb and Sons in New Brunswick under the direction of Tillman D. Gerlough and donated by him. The types II and V substances were sent to Maurice Stacey in Birmingham, England. It seemed of interest to determine the immunochemical differences and similarities between the type II and the types V and VI substances, as the latter types were "atypical IIs" designated IIA and IIB by Avery [5] and were later given type numbers of their own because of their frequent occurrence in pneumonia. Because of heavy, immediate cross-reactions of certain plant gums with nonreducing lateral end-groups of D-glucuronic acid in anti-Pn II, I had written Maurice that he would find such groups in the type II substance and fewer, or 1, 2-linked

¹Ogata was devoted to music and knew many of the local musicians. I asked him if he played any instrument. "Piano," he said without any evidence of rancor, "until my house was bombed." Western music was well understood and played. Besides playing with various groups, I went to Mischa Elman's rehearsal of the Beethoven and Mendelssohn concertos with the Tokyo Philharmonic. The conductor, at least, must have been studying Mischa's records, for at the end, Mischa, much moved, said: "This is the first time in my life I haven't had to stop an orchestra rehearsing these concertos." When Charlotte and I were in Tokyo in 1971, Ogata arranged for us to play chamber music in the reception room of a pharmaceutical company for which he was consultant. There was a grand piano, and the cellist was the company's chief chemist.

D-glucuronic acid, in that of type V. The prediction was confirmed for type II [6] and the second alternative for type V [7], which Maurice had assigned to a junior associate, S. Alan Barker, who discovered two previously unrecorded aminosugars in the substance. Paul and I found that the type VI polysaccharide resembled the teichoic acids of Baddiley, that it was the first naturally occurring polysaccharide of which a crystalline repeating unit could be isolated practically quantitatively [8, 9], and that its somewhat limited relationship to the type II substance was due to its 1, 3-linked α -L-rhamnose [10]. Later in this study we were joined by Esther Hurwitz of Rehovoth, Israel, who then went on to work with Michael Sela and Ruth Arnon at the Weizmann Institute. Alan Barker also came for a brief stay, helping with several projects (e.g., [11]). Kenneth Amiraian, who had started as a graduate student with Otto and me at P. and S., continued his research on complement [12] with us at Rutgers and was given his Ph.D. at Columbia. He is now a senior biochemist in the New York State Department of Health laboratories in Albany. Bertil Björklund, from the State Bacteriological Laboratory in Stockholm (to which he returned), also went with us from P. and S. and continued with the fractionation and cross-reactions of glycogen. An early visitor was Hans Jahrmärker of Munich, who also studied with us the immunochemistry of glycogen and amylopectin [13].² He is now a professor of medicine at the University of Munich, and we have visited him and Ursula in their home near that city. Another visitor was Giorgio Cavallo of Italy, who worked mainly with Otto on complement and hemolysis [12], became professor of microbiology at Turin's university, and is now Rector. To him I owe an honorary doctorate from his university and the warm reception and hospitality accorded Charlotte and me in that city. Then there was also Philippe Doat, from Perpignan, who learned our quantitative precipitin method in record time. Years later, we stayed in the beautiful home he and his wife, Aline, a pharmacist, occupied at Chateau Roussillon, near Perpignan, and had our first visit to the Pyrenees with them.

A more permanent co-worker was Mervyn J. How, from Stacey's department. He stayed for 2 years, with his wife, Hazel, working on the difficult polysaccharide of Pn I [14] and on a review, with Stacey as co-author, on Pn polysaccharides. Mervyn is now an official of Unilever near Bedford, and we have visited him and his family there. Then there was C. V. N. Rao, on leave from the Department of Macromolecules of the Indian Association for the Cultivation of Science in Calcutta, who stayed for several years and went with me to the medical school of New

²At the end of his stay Hans and his wife wanted to drive to the Pacific coast and back. I took him to all of the used car lots within reach, but prices were out of his reach. My ancient Oldsmobile at \$200 solved the problem. They made the trip with only one major breakdown and sold the car for \$30 to Cavallo, who had just arrived with his wife, Ornella.

York University in 1964. Rao started the work on the structure of the capsular polysaccharide of Pn IX [15], one of the types which had reacted strongly with polyglucoses, and also studied plant gums [16, 17] of South and Central America sent by Felix Cordoba of the University of Mexico, who had worked in the laboratory at P. and S. on cross-reactions of *Salmonella typhi* and *paratyphi* A and B in antipneumococcal sera and on the preparation of potent rabbit antisera to Pn types IX and XII [18, 19].

When all was running smoothly and several productive years had elapsed, Selman Waksman decided to retire as dean and director and maintain only his well-equipped office. Rumors of his intention caused lively discussions among the faculty, and suggestions and preferences for a new director were bandied about. A strong feeling prevailed that the faculty itself should have the privilege of choosing a new head. However, the institute was Selman's baby and his benevolent authority had never been disputed. He had already chosen Joseph O. Lampen, an active and promising young biochemist, and Lampen had accepted. Some of the faculty were enraged, others disappointed, but when the new director arrived he immediately called a meeting of the faculty, asked its advice, and handled the tense situation with such tact that all hard feelings rapidly subsided. Joe has been the director for 22 peaceful, harmonious years and only now (1980) has decided to step down in order to devote himself entirely to the research on enzymes he had kept going at the institute.

A trip to Jamaica resulted in the acquisition of Jean M. Tyler, originally from Sheffield, as a member of our group. Charlotte and I had gone there to spend a week with May Todd, widow of Edgar Todd, an English microbiologist who had worked at the Rockefeller Institute and had held other posts here. They had moved to Montjoy, a beautiful hilltop house, when Edgar's health began to fail. Two lectures at the University of the West Indies were also arranged through Prof. L. J. Haynes, head of its Department of Chemistry in which Jean Tyler was a lecturer. She asked to work on a Pn polysaccharide, and after I had sent her some crude type VII to purify, decided she would like to transfer to Rutgers. Jean became very active in our research [20, 21] and teaching programs, moving on eventually to Baddiley in Newcastle and then to a professorship in the Medical College of Georgia in Augusta, where we visited her just before a recent Federation meeting in Atlanta.

At Rutgers I sponsored the last of my Ph.D.'s. A very able graduate student from the Polytechnic Institute in Mexico City had worked for several years with Walter Nickerson, after which the Polytechnic's dean wrote and asked if I would accept a student. I answered, "Yes, if he is as good as the last one." And so he turned out to be. Sergio Estrada-Parra and his wife, Theresa (Teri) arrived with little knowledge of English.

Early problems of mutual understanding were soon past and we became fast friends. Sergio was assigned the Pn type XVIII substance, work on which had been started in the laboratory at P. and S. by Harold Markowitz. We isolated more material from a pound of pneumococci grown for us at Porton, England, where the then director, David Henderson, was a friend of Werner and Barbara Braun, at whose home we had met. Sergio was able to define two alternative structures for the type XVIII substance. It was the first Pn polysaccharide shown to have a glycerophosphate side-chain, and it also had an O-acetyl in the repeating unit [22]. Sergio, too, found that the polysaccharide of Pn type XVIII A (now LVI) had a similar composition, with N-acetyl-D-glucosamine in addition, and added to the knowledge of the streptococcal group A substance [23]. Returning to Mexico, he was soon made professor of immunology at the Polytechnic. At the first of two symposia at which we were guests, he produced a bronze plaque naming his department the "Michael Heidelberger Department of Immunology," just as if I had set it up with a million dollars! Sergio has just been made director of the Polytechnic's medical school—a pity, I believe, to convert a gifted investigator into an administrator.

The story of the 9 happy years at the Rutgers Institute would be incomplete without telling of the many delightful evenings at the homes of Werner and Barbara Braun, the Brysons, Joe and Miriam Lampen, Otto and Anne Plescia, and Selman and Deborah Waksman, to list our principal friends at the institute in alphabetical order. There were other activities as well: for many of those years Charlotte played in the Princeton Orchestra, once as viola soloist with Helen Tas, violin, in Mozart's Sinfonia Concertante. We also took part in chamber music at Walter and Hedi Koerber's home in Kingston and with friendly members of the Department of Music at Rutgers.

Rutgers, too, had been the first university in the United States to grant me an honorary degree (in 1961) although, strangely enough, four French universities had already done so. My French friends also managed to have me elected to the Légion d'honneur, although I have never been able quite to understand how or why. Possibly it was because, as representative of the National Academy of Sciences at memorial services for Jean Perrin, a noted French physicist, I was the only American who spoke in French.

During the last years at Rutgers service on the subway in New York deteriorated and I missed so many trains to New Brunswick as a result of slowdowns that it became too nerve wracking. Again luck was on my side, for friends at the medical school of New York University had heard that I might return to New York. The University Hospital had just been opened in 1963 and several laboratories had been vacated in the Department of Pathology in the Medical Science Building. Alexander S.

Wiener also kindly offered part of his large laboratory, but I chose two small rooms opposite each other on the pathology floor, where a broader range of immunological research was under way by the departmental head, Chandler A. (Al) Stetson and a young friend, Baruj Benacerraf, in whose apartment in Paris I had been a guest. The National Science Foundation, which had been supporting my work, agreed to the transfer, greatly simplifying matters.

Accordingly I bade reluctant farewell to my good friends at the Institute of Microbiology, knowing that this would not be a complete break. We often saw the Brauns, Lampens, Lechevaliers, and Plescias—the Brauns until Werner's sudden death and Barbara's not long after. I had the sad privilege of speaking at the memorial service for Werner. We still exchange visits with the Plescias, and Otto has asked me to give a lecture in almost every repetition of the course on immunochemistry.

A diversion which I surely owed to Maurice Stacey and Jim Baddiley occurred in 1960, when the Chemical Society of Britain asked me to give its Centenary Lecture. I talked on "Chemical Constitution and Immunological Specificity," varying the 10 scheduled lectures somewhat depending upon whether they were given in a department of chemistry or a medical school. Hospitality was warm everywhere, discussions were often lively, and I learned much from visits to colleagues in centers of activity such as Manchester, Newcastle, Hull, Oxford, Cambridge, and London, among others. In Dublin we were shown through the Guinness brewery and the adjoining research laboratories where the only restriction was "no interference with the brewmaster."

Another memorable journey started in May 1963 with a cruise around the Aegean Sea and visits to Greece which included a lecture at Athens arranged by an old acquaintance, Leonidas Zervas, professor of chemistry. From Athens we flew to Israel to participate in a symposium at the opening of the Life Sciences Building at the Weizmann Institute of Science in Rehovoth. Many of our friends were at the institute's guest house, there was also time for sightseeing and seminars at other centers, and Michael Sela, now president of the institute, and Ephraim Katchalski, then not yet president of Israel, were tireless in their hospitality. Again in Athens after an incomparable 4-day bus trip around Greece, we took off for lectures in Praha, where J. Sterzl was our sponsor, and in Zurich, where Arthur Grumbach and Hans Storck officiated. The Czech plane was unaccountably delayed out on the hot airfield at Athens, but we sweltering passengers calmed down as soon as we were airborne and the hostesses appeared with liberal glasses of cold Pilsener beer.

In 1964 the Child Research Council of Denver appointed me to a scientific advisory committee. In several highly interesting and instructive (to me, at least) visits to its offices and laboratories, I learned of the operation of their "from conception to the grave" program—its acquisi-

tion of vast quantities of measurements and data and its emphasis on individual variation. The few suggestions I could make had barely been adopted when the entire 40-year-old project collapsed tragically for lack of support.

After a visiting professorship of several months at the Faculty of Pharmacy of the University of Paris in 1957, I was asked to be a speaker at the Centennial of the Société de Chimie Biologique at the Sorbonne in 1964. I talked on "Contribution de l'immunochimie à l'étude des structures biologiques" [24], reading from a manuscript on which my friend Nine Choucroun, of the Institut Rothschild in Paris, spent hours converting it into idiomatic French and helping give each word the desired shade of meaning. Unlike the native speakers, who mostly rattled off their remarks at top speed, I made my talk an oration, and the audience responded appreciatively. In this decade Charlotte and I also had a fascinating and productive series of visits to colleagues in Brazil, Argentina, Chile, and Peru, and a short stay at Stanford University where I was Visiting Professor of Microbiology.

In 1965 Charlotte and I were again in Europe visiting colleagues and their laboratories in Amsterdam, Leyden, The Hague, and other centers, where I had not been for about 40 years. And in November, at the suggestion of Morris Scheraga, professor of microbiology, there was a stimulating trip to take part in the centennial of the University of Kentucky at Lexington. This also gave me an opportunity to visit relatives of my first wife, Nina Tachau, mother of our son Charles, in Louisville.

Rao and I began work at NYU with little delay. It felt good to be back again in the atmosphere of a medical school with its widely varying interests and problems, with its far-ranging discussions and contacts in the faculty dining room at lunchtime, and with its stimulating new departmental associates: Al Stetson, the chairman; Baruj and his group; Jeanette Thorbecke and her co-workers and students—all passionately extending the knowledge of cellular immunology; Zoltan Ovary, at home in all branches of immunology and with a profound knowledge of art, music, and musicians as well; Michael Lamm, busy with the immunochemistry of antibodies; Victor Nussenzweig, clearing up some of the intricacies of complement; Mildred Phillips, Ross Basch, Aaron Janoff, Marvin Kuschner, Bradley Bigelow, and others concerned more with other aspects of pathology. It was broadening, too, when Bill Paul and Ira Green were down the hall in Baruj's laboratory, and later when Julia Phillips-Quagliata joined the department from England. The departmental executive secretary, Chauncey Chow, was tireless in his efforts to help, and when Wilfred R. Haddad came from biochemistry to succeed him, he, too, proved to be a wise counselor and true friend. After Al Stetson stunned us all with his sudden decision to become dean of the medical school of the University of Florida at Gainesville, the new

chairman, Vittorio Defendi, proved to be equally friendly and helpful. I usually gave one or two lectures in the courses on immunology but did not accept any graduate students, not knowing how much longer I might be able to work.

The Eastern School for Physicians' Aides supplied an honor student, "Pat" Grosvenor, originally from Barbados, who learned our methods quickly and gave valuable help until his growing family required a more lucrative position. Rao returned to Calcutta and came back to NYU twice for several months to work with Michael Lamm. He was succeeded all too briefly by Prasenjit Chakravarty, a Ph.D. of Melville Wolfrom's. My next co-worker was Amalendu Das, of the Department of Chemistry of Calcutta University, and we worked together on the polysaccharides of types IX and XXV [25], the latter because the horse serum available had strangely shown cross-reactions quantitatively greater than the homologous one. Established scientists who came for a few weeks to ensure the accuracy of their quantitative precipitin technique were Edward Jeska, professor of veterinary science at the University of Iowa at Ames, and Cornelius (Neil) P. J. Glaudemans of the Carbohydrate Laboratory at the National Institutes of Health. Strong friendships developed with both, and synthetic aldobiouronates made by the latter and a co-worker were essential for quantitative inhibition tests that disproved a proposed structure for the Pn type II polysaccharide [26].

Exciting days in the laboratory followed the arrival of William F. Dudman from Canberra. This experienced biochemist-microbiologist brought samples of the extracellular polysaccharides from strains of *Rhizobium trifolii* from "down under." He had been unable to methylate the substances as fully as usual, nor could he account for their greater acidity than calculated from their content of glucuronic acid. These polysaccharides were important because they could combine with the lectin-like substances of leguminous roots and so were thought to account for the specificity of strains of *Rhizobia* for certain plants. It seemed evident that something was blocking a portion of the sugar hydroxyls. We looked first for acetyl and found it, but not in amounts large enough to account for the discrepancies. Then Bill remembered that pyruvic acid had been found in a polysaccharide from another soil bacterium, *Xanthomonas campestris*. So we looked for pyruvic acid and there it was, 8–10 percent! But this was not all: the intact rhizobial substances had shown virtually no cross-reactions in anti-Pn sera until we reached type XXVII. We therefore asked Rachel Brown for some type XXVII polysaccharide, and it proved to be the first of the Pn substances in which pyruvic acid was found. Another surprise: Wolfgang Nimmich, of Rostock, began sending K (capsular) polysaccharides of *Klebsiella*, and one of them, K32, in which pyruvic was the only acid, not only precipitated anti-Pn XXVII but also anti-Pn IV. Again, we found about 8 percent of

the acid in the type IV polysaccharide. But was the acid immunologically important? Its removal not only drastically reduced homologous precipitation but also, with the rhizobial substances, led to cross-reactivity in several of the lower-numbered anti-Pn sera [27]. This was to be expected from the liberation of two sugar hydroxyls that had been blocked by the acetal ring formed by the keto-group of pyruvic acid. It still amazes me that pyruvic acid, so important in the metabolism of practically every living cell, can be even an immunodominant group when attached to two sugar hydroxyls in the repeating unit of a polysaccharide.

In the summer of 1969 I had lectured in Maurice Stacey's Department of Chemistry. Afterward John D. Higginbotham, who had just received his Ph.D., asked if he might come to work in the laboratory. He and his wife, Elaine, arrived shortly afterward and found a furnished apartment on West End Avenue, at which Charlotte and I listened occasionally to their records of Bruckner's symphonies, of which John was fond. Though of youthful appearance and slight of build, John was a prodigious and able worker. He was soon determining the composition, properties, and structure of the Pn type IV and IX specific polysaccharides, making full use of a gas chromatograph which Herbert Kayden, a professor of medicine, kindly allowed us to use in his laboratory in the adjoining hospital. The type IV substance contained D-galactose, and the N-acetyl derivatives of D-galactosamine, mannosamine, and fucosamine, and its pyruvyl group appeared to be exclusively on the galactose [28, 29]. Removal of pyruvyl was relatively easy, and this resulted in an astounding change of specificity. The type-specific substance became group-specific, precipitating nearly all of the antibodies to the group-specific Pn C polysaccharide in a number of anti-Pn sera. These relationships were worked out with the assistance of Emil C. Gotschlich, of Rockefeller University, who had been working on the C-substance [30]. The reason for this close correspondence is still not clear, as N-acetyl-D-galactosamine seems to be the only common feature in the type IV and C substances. Neither does phosphorylcholine, said to be immunodominant in the latter, occur in the former.

In the meantime Pat, our technician, was succeeded by an also-competent Chyang T. Fang who had won his B. S. from the University of California and who went on after about 2 years to do research with the American Red Cross in Washington, D.C. John Higginbotham returned to England for a brief stint in Bath and then became group leader in research on polypeptide substitutes for sugar at Tate and Lyle in Reading. When Charlotte and I went to spend a weekend at his home out in the country near Reading I looked in vain for John at the station until I penetrated the disguise of a bushy brown beard that made him appear 10 years older.

In September of 1966 we embarked on our first trip down under at

the invitation of Derrick Rowley, professor of microbiology at the University of Adelaide who had been a visitor in the laboratory at P. and S. as a Commonwealth Fellow; Sir Macfarlane Burnet, then director of the Walter and Eliza Hall Institute in Melbourne; and Gustave Nossal, now its director and long a friend. I had first met the Burnets in 1954 when Sir Macfarlane and I received the Behring award and again when he was chairman of a meeting in Geneva of chairmen of a number of panels that had labored to set up a policy on immunology for the World Health Organization. At that meeting we differed rather sharply over one point that he made, but he bore no ill will. I also wrote a rather unfavorable review of his theory of clonal selection and still blush when I think how wrong I was.

After a brief stay in Honolulu to lecture and see the A. A. Benedicts, we flew on to Brisbane and were agreeably surprised to hear our name called at the airport. Gus had alerted John Sprent, professor of parasitology at the university, and he drove us to our hotel and invited us to his ranch. There we met his wife and daughter and saw our first kookaburra. He also took us to a koala sanctuary (we thought he had said "cemetery") where Charlotte was photographed reluctantly holding one of those charming little animals in her arms. I lectured in Sprent's department and we flew to Cairns for a boat trip to Green Island on the Great Barrier Reef, with its astounding underwater sights. Next, there were several lectures to be given in Sydney. Contacts with Kenneth W. Knox, now director of the Institute of Dental Research there, have continued. In Canberra we lived in the fine guest house of the National University, visited the Dudmans before Bill came to the laboratory at NYU, and spent a day out in the "bush" with Alexander Ogston. The night we were to have dinner with Dr. Fenner and his wife he came to drive us to their home, only to find his usual route and a much longer alternative blocked by the police. Our President Johnson was in Canberra and security measures made traffic wait until he passed by. He was late and we were *very* late for dinner. In Melbourne there were lectures, visits to the Walter and Eliza Hall Institute, the University of Melbourne and Monash University, and excursions to the environs with the Adas and Nossals and to the seaside home of the Rodwells, as well as pleasant evenings in the homes of our friends.

Around Adelaide the hills were purple with a weed that had once saved flocks of sheep during a severe drought. Derrick had promised to have kangaroo anti-Pn II serum available, but this time luck was bad, for the period of immunization had been very wet, two of three animals had died of fungal disease, and the third became so savage that no one dared inject or bleed it. There was only an opossum serum, and it was very weak. However, during a stay of about 2 weeks I helped put the department's quantitative precipitin technique on the right track and gave

several lectures and seminars. The Rowleys were very hospitable, as were also the Charles Jenkins, of the department, and others of the faculty.

At almost every stop in Australia we took part in chamber music with members of the local faculty or else went to concerts by the Amadeus Quartet, which had much the same itinerary as ours.

At Hobart the University of Tasmania's people were also warm and friendly. There, too, we played with local musicians after my lecture. Strangely enough, to fly to New Zealand we had to return to Australia, as there was no direct air service. After sightseeing in Christchurch, the jumping-off place to the Antarctic, and after a 4-day bus trip to the Mt. Cook region and Queenstown, work began at Dunedin with visits to the laboratories where a virus that had afflicted sheep was being studied. Then there was a lecture in John Miles's Department of Microbiology at the university, followed by several trips through the beautiful countryside with John and his wife, Ruth. Then we were off to Palmerston North for a lecture at the young Massey University. There our sponsor was Donald F. Bacon, who had been at the Waksman Institute of Microbiology. At Wellington there was a lecture at the Royal Hospital and finally another, as well as music, in Auckland, from where we flew to Hawaii and home—after 21 lectures and seminars and an incredibly interesting and stimulating trip.

Near Canberra there was an Animal Research Station whose director, Mervyn Griffiths, was an authority on the strange Monotremes. He introduced us to one of them, the echidna, a small, spiny anteater that waddled along, lapping up ants with its long, slimy tongue. It seemed to me that a slime with so special a function ought to be different from other sublingual secretions. When Jow Y. Lew came to the laboratory in New York after winning his doctorate at the University of California at Riverside, we studied samples sent by Griffiths, but they turned out to be surprisingly like the canine substance [31]. Jow also found that the pyruvyl group in the Pn type IV polysaccharide was attached to positions 2 and 3 of D-galactose [32] and was therefore probably under strain. This would explain its easy removal.

A long-continuing investigation began in 1963 when I received an acidic polysaccharide of a strain of *Aerobacter aerogenes* (later *Klebsiella* serotype K81) from a scientist in Kiel. It had been isolated and purified by Wolfgang Nimmich of the Institute for Medical Microbiology and Epidemiology of the University of Rostock. There are about 80 K (capsular) types of these gram-negative rods, just as there are roughly the same number of the gram-positive Pn types. From the rather limited cross-reactions of K1³ in anti-Pn sera I could make modest predictions of how a chemical investigation might place the sugars in the substance. It

³K with the appropriate Arabic numeral is used instead of "K polysaccharide."

seemed of interest to compare the cross-reactivities of these two extensive phylogenetically widely separated families of microorganisms. Nimmich eventually prepared and sent the entire series of *Klebsiella* Ks and several Os as well. There was a surprisingly large number of cross-precipitations in anti-Pn sera, and the strong reactions were measured quantitatively [33]. Guy G. S. Dutton of the University of Vancouver began structural studies of the Ks, as did also Stephan Stirm of my friend Otto Westphal's Max Planck Institut für Immunbiologie in Freiburg, Bengt Lindberg of the University of Stockholm, and others. I was often able to tell them, as a result of rapidly developing, massive precipitin tests in anti-PnII serum, for example, that they would find D-glucuronic acid in a K as lateral, nonreducing end-groups, or, with anti-Pn XXIII serum, one could identify similarly placed L-rhamnosyl residues. As more than 20 of the Ks precipitated anti-PnII strongly, it appeared likely that many in this group would cross-react in antisera to the reacting *Klebsiella* types and that these antisera might even precipitate the Pn II polysaccharide. These possibilities became actualities with rabbit antisera supplied by Jorunn Eriksen, who had studied *Klebsiella* for many years at the Rikshospital in Oslo with Sverre D. Henriksen [2, p. 10]. Also useful were the anti-K7 and anti-K11 sera of Stephan Stirm of Freiburg, as well as a pool of rabbit anti-K2 sera which Soo Hoo [2, p. 3] and I had raised in 1934. *Klebsiella* K47 gave the heaviest precipitation in the smaller group of Ks highly reactive in anti-Pn XXIII serum, and two different anti-K47 sera of Jorunn's cross-reacted with most of these Ks [34, 35]. It is therefore clear that many of the *Klebsiella* serotypes can be grouped into chemotypes based on the nature and position of an immunodominant sugar much as Otto Westphal, Otto Lüderitz, and their co-workers have done with *Salmonella*. I have lectured several times at their institute in Freiburg, studied cross-reactions of a number of *E. coli* polysaccharides prepared by Klaus and Barbara Jann [36], and of other material sent by Hubert Mayer and Stephan Stirm (see above)—all members of the institute's staff. And Charlotte and I can attest to the warm hospitality, over the years, of Otto Westphal and his first wife, Olga, and later, his second wife, Uschi, and to the many sessions of chamber music listened to and participated in with Otto, an accomplished flutist, and his friend, the musicologist Fritz Neumeyer. With "Onkel" Fritz at a piano of Mozart's time we played the Mozart trio for clarinet, viola, and piano.

After the First International Congress of Immunology in 1971 we made our first trip around the world. We had long planned to visit relatives of Charlotte's in Nairobi, and I was scheduled to give two lectures in Ames at the invitation of Paul Rebers and Ed Jeska. As it seemed almost as easy to keep on going from Nairobi to Ames as to return to New York and then fly west, we chose the spectacular route, in part with

the assistance of the Rockefeller Foundation (luck again!) which was especially interested in the Veterinary College near Nairobi. I visited and lectured in the medical school and hospital in both Kampala and Nairobi and in the above-mentioned Veterinary College before an exceptionally eager and well-trained body of students and faculty, and we flew with Susanna (Charlotte's cousin) and Bob Markham to the Samburu game park after going from Kampala to Murchison Falls and to the huge Ngorongoro game park. Then Bombay, with a side trip to Poona to visit the Venkataramans and lecture at the National Chemical Institute and New Delhi to enable Charlotte to see the Taj Mahal at Agra. Then to Bangkok for a lecture, Osaka to see the Amanos again and lecture in his Institute, Kyoto where sightseeing was made easy by members of Amano's staff who came from Osaka each day, Nara, and Tokyo, where I lectured again in Ogata's old department, headed since his retirement by Kan Suzuki. And finally Ames, the excuse for all this, with its fine campus and staff and its cordial hospitality.

The second International Congress of Immunology in Brighton in 1974 supplied a welcome opportunity to confer with our English and European friends again, and in October 1976 I had a poster in French at the Congrès Francophone International d'Immunologie at Pointe-au-Pic, Quebec, on the St. Lawrence River. About 150 French-speaking immunologists came from Europe to join their North American colleagues for a highly concentrated and successful meeting in a single large hotel. And in the summer of 1977 another memorable occasion was the four-hundred-fiftieth anniversary celebration of the University of Marburg with its panel on immunology and the unfailing hospitality and friendship of Gerhard Schwick, director for research at the Behringwerke, and his wife Ruth. Impressive, also, was the joint German-Israeli biological congress held at Göttingen and Braunlage in 1978 for which I was asked to give an historical talk. There the chairman, Manfred Eigen, opened the proceedings not with a speech, but with a Mozart piano concerto, which he played superbly with a small orchestra.

A joyful surprise was New York University's celebration of my eightieth birthday with a citation from its president and a dinner to which friends came from many miles around. This was followed by a concert beginning with a modern "Happy Birthday" by John Corigliano, commissioned by Zoltan Ovary. In subsequent years there were dedicatory numbers of two journals and articles in others. And lately, for my ninetieth, NYU held a special convocation at the Medical Center at which President John Sawhill presented me with a D.Sc. and Ivan Bennett presented Charlotte with a huge bunch of red roses. The convocation was followed by chamber music for clarinet (Zoltan was again the impresario) and a reception.

In the autumn of 1977 my calcified and leaking aortic valve forced me

to enter the University Hospital just before I was scheduled to lecture at Columbia and share the Louisa Gross Horwitz award with Elvin Kabat and Henry Kunkel. However, luck was with me again, for my son Charles accepted the award for me and Frank Spencer, head of our Department of Surgery, was willing to give me a new valve in spite of my age, and so skillful were the surgeon and the anesthetist, Peter Walker, that I was back in the laboratory again in 6 weeks.

When my NSF grant expired in 1976 after a number of renewals I did not ask for another extension because younger workers were increasingly becoming casualties of the vast sums our government was spending on ever-more-lethal weaponry. With my large stocks of antisera and polysaccharides I could go on indefinitely without additional funding provided NYU continued generously to furnish space amid stimulating, helpful colleagues [37]. There is so much more to do!

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THE TREE IS THE SEED'S WAY OF MAKING ANOTHER SEED

Lying dormant year 'pon year,
Bravely shedding ne'er a tear,
Lies the seed snug in its coat,
Be it jackpine, oak, or oat.

But fire or flood ends inhibition,
Pores open wide for imbibition.
Then radicle, shoot, and cotyledon,
Soon stores are spent, it's time for feedin'.

Break through the ground; now there's the sun!
Life's energy, the first goal's won.
True leaves now, and stem, and root,
Then the goal toward which all shoot.

Flowers, bees, and pollination;
Thus, the end of a generation:
New seed is set, and peace will reign,
For dormancy is come again.

JOHN R. PRINGLE